

### Remarks and Arguments

Claims 8-17, 19 and 20 were objected to under 37 C.F.R. §1.75(c) as being in improper dependent form due to the mention of four terminating NTPs in each of Claims 8 and 10. These claims have therefore been amended to correct for this oversight by referring instead to “a complementary mixture of terminating and non-terminating nucleoside triphosphate derivatives.” This phrasing is certainly within the scope of the original claim language and, therefore, supported by the application as originally filed. Reconsideration of Claims 8-17, 19 and 20 under this ground for objection is respectfully requested.

Claims 1-5 and 7-29 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In particular, the examiner has argued that the language “said mixture having a ratio of one non-terminating to three terminating nucleoside triphosphate derivatives, or two non-terminating to two terminating nucleoside triphosphate derivatives” of Claim 1, and the language “a complementary mixture of fewer than four non-terminating and terminating nucleoside triphosphate derivatives” of Claim 24, is not described in the specification. However, although the language may not be found verbatim in the specification, there is ample support in the specifications for these concepts, and one of ordinary skill in the art would have no difficulty recognizing them.

Paragraph [0052] of the applicants’ specification includes the following passage:

Next, apart from the extension primers with phosphorothioate bonds at the end, which have been provided with linkers according to the invention, a *reduced set* of modified deoxynucleoside triphosphates (such as  $\alpha$ -S nucleotides or  $\alpha$ -Me nucleotides) are added, in which the nucleotide is missing at which the chain extension specifically for the mutation should stop. (emphasis added).

Use of the term “reduced set” clearly establishes that a set of fewer dNTPs may be used for primer extension. Two sentences later, paragraph [0052] states that:

As an extension to this, one or more dideoxynucleoside triphosphate terminators can be added which do not exist as deoxynucleoside triphosphates.

By adding one or more ddNTPs to the reduced set, in particular those that “do not exist as [dNTPs],” the disclosure is specifically describing dNTP/ddNTP sets that fall either within the scope of Claim 1 or within the scope of Claim 24.

A few examples may be used to demonstrate how the language of the applicants’ disclosure provides clear support for each of Claims 1 and 24. If a “reduced set” includes just one dNTP, and three ddNTPs are added, the dNTP/ddNTP ratio would be 1:3. If the reduced set consisted instead of two dNTPs, and two ddNTPs were added, the resulting ratio would be 2:2. These, of course, are the ratios that are specifically recited in Claim 1.

Of course, the language of paragraph [0052] is also consistent with Claim 24. If the reduced set of dNTPs has added back to it a number of ddNTPs that keeps the total number below four, this would obviously be a “complementary mixture of fewer than four non-terminating and terminating nucleoside triphosphate derivatives.” For example, if the reduced set has one dNTP, and two ddNTPs are added to it, the result is a complementary mixture of fewer than four terminating and non-terminating NTPs. The same would be true for a starting set of two dNTPs to which is added one ddNTP. Thus, the necessary support for Claim 24 is also present in the application.

In considering whether the written description requirement under 35 U.S.C. §112, first paragraph is met, “the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed” (*Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). As discussed above, the applicants were clearly in possession of the invention as now claimed at the time the application was filed. The excerpts discussed give a clear example of how one skilled in the art would obviously understand the invention to

include the use of the dNTP/ddNTP ratios recited in Claim 1, as well as the complementary mixture of fewer than four dNTPs and ddNTPs as recited in Claim 24. And, although the language of the claims is more detailed, the concepts are fully supported by the specification. As noted in MPEP §2163.02 “[t]he subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement.” Since the subject matter of the claims falling under this rejection was properly recited in the applicants’ specification, as filed, reconsideration of Claims 1-5 and 7-29 is respectfully requested.

In light of the foregoing amendments and remarks, it is respectfully requested that all of the claims be allowed such that the application may be passed to issue. If it is believed that a telephone conference will expedite prosecution of the application, the examiner is invited to call the undersigned. The Commissioner is hereby authorized to charge any fees due for the filing of this paper to the applicants' attorneys' Deposit Account No. 02-3038.

Respectfully submitted

Philip L. Conrad  
Philip L. Conrad, Esq. Reg. No. 34,567  
KUDIRKA & JOBSE, LLP  
Customer Number 021127  
Tel: (617) 367-4600 Fax: (617) 367-4656

Date: August 29, 2005